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Penn Vet Faculty for the Future

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Drs. Mark Oyama and Meg Sleeper examine a patient. Photo by John Donges.

It's all about heart—at least, that is, for **Dr. Mark Oyama**, associate professor of cardiology, and **Dr. Meg Sleeper**, chief of the Cardiology Section of the Matthew J. Ryan Veterinary Hospital. Their research into diagnosing and curing heart disease can benefit not only the dogs that are the focus of their work, but also people—whose hearts, literally and figuratively, already benefit so much from their connections with these quintessential companion animals.

Like people, dogs can suffer from both congenital and "acquired" heart disease—and even with the development of new technology and medications, even with an ever-broadening knowledge base about the causes and courses of heart disease, illness and death in dogs with heart problems remains high. According to the American Veterinary Medical Association, approximately 3.2 million dogs in the United States that have annual veterinary examinations suffer from some form of acquired heart disease and may be in heart failure. And because of the genetic similarities between dogs and people, the study of many congenital defects that affect one species can lead to breakthroughs with both.

Dr. Oyama has studied how stem cell research might be used to treat dogs with heart disease. Before he came to Penn from the University of Illinois College of Veterinary Medicine in 2005, he investigated how damaged heart cells in dogs could be repaired by transplanting the animals' own stem cells into their hearts—a process known as cardiac cellular transplantation. But the fundamental biological processes that govern the behavior of these cells remains a mystery, as does the long-term efficacy of the procedure.

"I think people get excited about it because of the huge potential that it has," Dr. Oyama says. "Even in people, it's an area about which very little is known. When they're doing stem cell transplants in people, yes, it appears to improve the heart function, but when you ask the scientists 'How is it doing that?' nobody knows. They don't have any idea. Cells go in there, and somehow they're making the heart function better."

Cardiac cellular transplantation could have a marked effect in treating dilated cardiomyopathy, or DCM, the second-most-common acquired heart disease in dogs. Some large breeds, such as Dobermans, great Danes and boxers, are particularly prone to it. DCM causes the heart muscle to lose strength and fail to pump blood properly, and can eventually lead to heart failure. To identify genes that may play a role in the process of the disease, Dr. Oyama and his colleagues used a commercially available gene chip, or microarray, designed for dogs—a 1.5-inch square that contains more than 23,000 genes. When exposed to the genetic material from Doberman dogs that had died from heart disease, genes on the chip lit up if they were active in the sample. The researchers knew the nature and location of the genes on the chip, so they could identify the active genes in the samples and determine their level of activity by the brightness of the fluorescence. Essentially all 23,000 genes, tested at once, were narrowed down to 167 genes that could play a role in the development of DCM.

Dr. Sleeper, too, has focused on DCM in dogs—but her work primarily has been on treatment. "My primary research interest is therapeutic gene transfer," says Dr. Sleeper. "Basically, with the procedure in which I am interested, we inject genetic material into the patient's myocardial cells using a catheter-based approach and a virus, which is not capable of replicating (infection). These cells then produce the gene product: one of several proteins that improve myocardial function. We currently are in the process of proving safety, and once that is complete, my goal is to offer this technique as a therapeutic option for dogs with DCM." The procedure also offers great potential for humans—and in late 2008 Dr. Sleeper spent time in China treating monkeys to evaluate its feasibility in non-human primates.

A paper published recently in the *Journal of the American Veterinary Medical Association* (Vol. 233, No. 1, July 2008) and co-authored by Drs. Oyama and Sleeper, as well as **Dr. Dottie Brown**, associate professor of surgery and associate director of the Veterinary Clinical Investigations Center at Ryan Veterinary Hospital, and other colleagues, attempts to better define the importance of quality versus quantity of life in dogs and cats with heart disease. Probably the first investigation of these issues, the report reveals that successful treatment of heart disease in dogs must acknowledge owner's perceptions and priorities with regard to their dogs' quality of life.

"What is more important to owners?" asks Dr. Oyama. "Do they value long life or high quality when forced to reach a balance between the two?" The paper finds that owners of dogs with cardiac disease highly value their pets' quality of life—and that veterinarians need to address these issues to ensure that the care provided is directed toward the desired goals. Furthermore, veterinarians should continue to help owners reassess their priorities as their pets' clinical circumstances change. Clinical trials similar to those carried out by the Veterinary Clinical Investigations Center in which therapies for heart disease in dogs are tested should include quality-of-life concerns as endpoints, and future studies also should seek ways to better measure these goals.